Application and Validation of Biomarkers
→ Use of Biomarkers

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What I've heard

- Validation vs. Qualification
  - analytical validation
  - clinical qualification
- Biomarker → Genomic Test → Pharmacogenomic Test ~ must be clinically meaningful
- Bridging
  - platform 1 → platform 2
  - preclinical → clinical biomarkers

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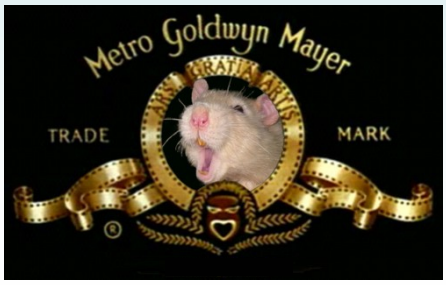
What I've heard

- Toxicogenomics: cost/benefit
  can we replace costly tox studies with less costly and much faster toxicogenomic studies?



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What I've heard

- Increasing complexity of biomarkers:
  DME → Molecular Targets → Tissue Injury Model → Pattern Recognition ~ ideally: combine multiple markers

- Pattern recognition:

  use of biomarkers in clinical setting done since many years (it's the physician's job) ~ longitudinal observations

  use of new biomarkers (genomics, proteomics, others) as a snapshot represents patterns ~ but how can we recognize and use them

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What I've heard

- Need for consortia:

  validation (probable to known valid) of biomarkers is too complex for individual entity to perform, requires cross-validation

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What I've heard

- Co-development:

  rely more on drug development program to provide the evidence of clinical utility for tests ~ when?

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What I've heard

- New breed of artists: molecular pathologists

  for example, today they recognize what tissue they have in front of them based on gene expression profiles ~ does it evolve into disease recognition, efficacy?

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What I've heard

- Move away from black & white

  need to move away from extreme views and put genomics into perspective ~ for example, better define sensitivity and specificity of pharmacogenomic tests, justify incremental cost with clear benefit, i.e. clinical utility (Amplichip)

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What I've heard

- Biomarker performance is about risk management

  quantitative risk models
  decision making
  redefining disease

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What I've heard

- New statistical approaches will open up new ways to conduct clinical trials, for example:

½	0.4	All comers
½	0.1	Biomarker
1	0.5	

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What I've heard – Wish List Sent to FDA

- New guidances
    1. Drug-Test Co-development
    2. Statistical Considerations
    3. Biomarker Qualification
- List of genomic biomarkers on website

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Different View ~ Business of Using Biomarkers: Herceptin®

Trial Design	With HER2 neu	Without
# of patients	470	2200
Response rate	50%	10%
Years of follow-up	1.6	10

- Savings in clinical trial costs ~ $35 million
- Income from 8 year acceleration of product ~ $2.5 billion
- Access to drug from acceleration ~ 120,000 patients

After Press and Seelig, Targeted Medicine 2004, New York, November 2004

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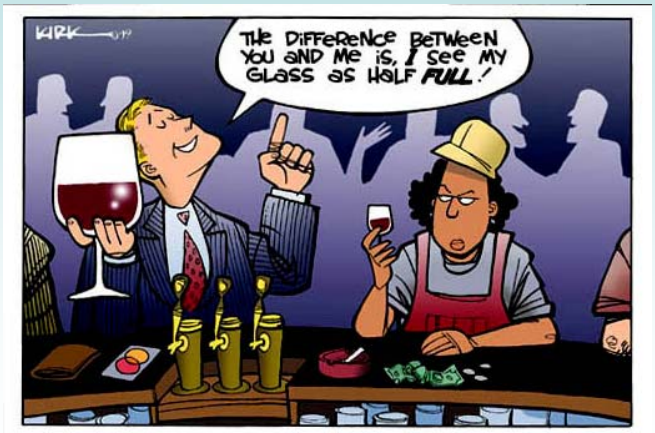
New (Genomic) Biomarkers: Modesty – Realism – Robust Optimism



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www.fda.gov/cder/genomics